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Published in:
EBioMedicine

DOI:
[10.1016/j.ebiom.2015.12.019](https://doi.org/10.1016/j.ebiom.2015.12.019)

Publication date:
2016

Document version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Keogh-Brown, M. R., Jensen, H. T., Arrighi, H. M., & Smith, R. D. (2016). The impact of Alzheimer's disease on the chinese economy. *EBioMedicine*, 4, 184-190. <https://doi.org/10.1016/j.ebiom.2015.12.019>



Research Paper

The Impact of Alzheimer's Disease on the Chinese Economy

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ARTICLE INFO

Article history:

Received 8 October 2015

Received in revised form 11 December 2015

Accepted 21 December 2015

Available online 22 December 2015

Keywords:

Macroeconomic

Modelling

Alzheimer's Disease

China

ABSTRACT

Background: Recent increases in life expectancy may greatly expand future Alzheimer's Disease (AD) burdens. China's demographic profile, aging workforce and predicted increasing burden of AD-related care make its economy vulnerable to AD impacts. Previous economic estimates of AD predominantly focus on health system burdens and omit wider whole-economy effects, potentially underestimating the full economic benefit of effective treatment.

Methods: AD-related prevalence, morbidity and mortality for 2011–2050 were simulated and were, together with associated caregiver time and costs, imposed on a dynamic Computable General Equilibrium model of the Chinese economy. Both economic and non-economic outcomes were analyzed.

Findings: Simulated Chinese AD prevalence quadrupled during 2011–50 from 6–28 million. The cumulative discounted value of eliminating AD equates to China's 2012 GDP (US\$8 trillion), and the annual predicted real value approaches US AD cost-of-illness (COI) estimates, exceeding US\$1 trillion by 2050 (2011-prices). Lost labor contributes 62% of macroeconomic impacts. Only 10% derives from informal care, challenging previous COI-estimates of 56%.

Interpretation: Health and macroeconomic models predict an unfolding 2011–2050 Chinese AD epidemic with serious macroeconomic consequences. Significant investment in research and development (medical and non-medical) is warranted and international researchers and national authorities should therefore target development of effective AD treatment and prevention strategies.

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1. Introduction

The last century witnessed dramatic global improvements in life expectancy and quality of life. However, since dementia primarily affects those aged over 60, increased longevity has led to increased rates of dementia and, more specifically, its most common form, Alzheimer's Disease (AD) (Prince et al., 2009). AD represents 42–81% of dementia cases (Nussbaum and Ellis, 2003), and is characterized by progressive, global deterioration of intellect, including memory, learning, orientation, language, comprehension and judgment. It affects the ability to

perform everyday activities (ADI, 2014), causes distress to patients and their close contacts, creates extra demands on health systems, and imposes a substantial burden of long-term care (Wimo et al., 1999). There are currently no effective treatments or interventions to mitigate AD progression, and the incidence rates for AD double every 5 years from age 65 (Brookmeyer et al., 1998). The global burden of AD is therefore expected to accelerate in the face of reductions in mortality from other conditions: from 26.6 million cases in 2006 to 106.8 million by 2050 (Brookmeyer et al., 2007). Some evidence suggests that incidence rates for AD in the US and Europe may have declined in recent years (Matthews et al., 2013; Qiu et al., 2013; Langa, 2015), possibly due to reduced exposure to minor life-style related AD risk factors such as obesity, diabetes and smoking (Langa, 2015; Satizabal et al., 2014). However, dementia and, by implication, AD, has been highlighted as a particular concern for China (Sousa et al., 2009), since life-style risk factors are currently increasing with growing income-levels and since the on-going demographic transition combined with the demographic profile means that the primary risk factor for AD, aging, will drive future increases in Chinese prevalence. Chinese life expectancy increased from 70.0 to 75.2 during 1993–2012 and population estimates (USCB, 2014) suggest that the proportion of the Chinese population aged 60

Abbreviations: AD, Alzheimer's Disease; NPV, Net Present Value; GDP, Gross Domestic Product; COI, Cost Of Illness; RMB, Renminbi; DALYs, Disability Adjusted Life Years; YLL, Years of Life Lost; YLD, Years Lived with a Disability; CGE, Computable General Equilibrium; GTAP, Global Trade Analysis Project; SAM, Social Accounting Matrix; CDR, Clinical Dementia Rating; PADL, Personal Activities of Daily Living; IADL, Instrumental Activities of Daily Living; p.a., per annum.

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and over, the ages at which onset of Alzheimer's Disease is most likely, will increase from 12% in 2010 to 33% by 2050.

In addition to the burden on the population, it is hypothesized that the considerable health and care burden of AD will impose a large economic burden throughout affected economies. Previous economic studies estimate the 2009 worldwide cost of dementia to be US\$421 billion and attribute 10% of the global burden (US\$41 billion) to China (ADI, 2009). Shanghai-specific per patient costs of AD were estimated to be 19,001RMB (US\$2,384; 2006 prices) (Wang et al., 2008). However, indirect (unpaid) caregiver costs (56%) drive the cost estimates and all previous estimates are formed by using a Cost-of-Illness (COI)-based method to scale direct patient-specific and indirect caregiver and medical costs by the number of cases. Existing estimates of AD therefore ignore the wider spillover and interaction effects for the economy, in general, and the extent to which these compound over time, and they also commonly monetize caregiving time by non-workers. Over and above the economic effects across sectors, the predicted scale of the future Chinese AD health and economic burdens suggests that Chinese labor markets may be affected. The combined interactions of China's predicted economic development, increased proportion of elderly workers, excess labor availability (Das and N'Diaye, 2013), and health and caregiver burdens over time, will affect labor supply and wage levels in a way which previously employed methodologies cannot accurately predict. These dynamic impacts, which are the fundamental units by which health and care effects should be valued, can only be estimated using a macroeconomic multi-sector approach and yet no studies of this nature have yet been conducted for AD or, more broadly, for dementia.

A multi-sector macroeconomic simulation model is employed in this study together with an epidemiological model of AD. The dual macroeconomic and disease simulations are employed to consistently estimate the twin macroeconomic and health burdens of AD in China from 2011 to 2050. The macroeconomic simulations focus on the accurate estimation of dynamic labor supply and wage effects of AD health and care burdens on working individuals whilst population-wide AD health and care burdens are assessed in parallel with the macroeconomic effects and include the health and care impacts that fall outside the labor force. The methodology employed to produce this holistic assessment is outlined in the next section.

2. Methods

2.1. Study Design

The analysis presented in this paper employs a double-simulation model framework consisting of an epidemiological model of AD progression and a macroeconomic Computable General Equilibrium (CGE) model of the Chinese economy for 2011–2050. China is a complicated country to undertake AD assessment given its rapid development, aging population and changing labor market structures, but the CGE model captures all relevant labor market structures as well as public and private health budget shocks, including the burgeoning cohort of 60–70 year old workers, creating potential for dramatic increases in the proportion of retired dependents with AD.

2.2. Alzheimer's Disease Model

A multistate probabilistic simulation model of AD progression (Brookmeyer et al., 2007, 1998; Johnson et al., 2007; Colantuoni et al., 2010) was used, based on Chinese population projections (USCB, 2014), age and gender-specific projections of Chinese mortality rates (Banister and Hill, 2004) and age-specific exponentially growing projections of AD incidence rates from age 60 (Brookmeyer et al., 2007) to forecast the number of Chinese individuals who contract AD. Whilst incidence grows exponentially with age, age-specific incidence rates are conservatively assumed to remain fixed over time. Co-morbidities

of AD patients were not explicitly accounted for, but are implicitly captured in the mortality rates.

Two stages of AD were simulated. Stage 1 corresponds to mild or moderate disease, and stage 2 corresponds to severe disease, as defined by the Clinical Dementia Rating (CDR) scale (Morris, 1993). Full discussion of the AD progression model is included in Appendix 1. The 11% annual transition probability from stage 1 to stage 2 (Brookmeyer et al., 2007) mirrors the observed transition from moderate AD to nursing care (Neumann et al., 2001) and is consistent with the six year average transition from detection to nursing care requirement (Stern et al., 1997). Similar to previous AD model applications (Brookmeyer et al., 2007), baseline simulations assumed no excess mortality for stage 1 patients but an annual 11% excess mortality rate for stage 2 patients. Previously established AD disability weights (Colantuoni et al., 2010; Stouthard et al., 1997) were used to estimate Years Lived with Disability (YLD) effects.

2.3. Economic Model

The economic model used in this study was a macroeconomic Computable General Equilibrium (CGE) model (Löfgren et al., 2002). CGE models have been used successfully in health-related assessments of pandemic influenza outbreaks (Smith et al., 2009), dietary change (Lock et al., 2010), and environmental change (Jensen et al., 2013) and a similar approach is applied here to assess the AD economic burden. In particular, attention is given to both improved simulation of future labor market wages at which economic burdens are assessed utilizing literature-based predictions that excess unskilled labor supplies may continue until 2025 (Das and N'Diaye, 2013) and separation of economic and non-economic impacts (monetizing only informal caregiver time by employed caregivers). The analysis of economic impacts is enhanced by using Net Present Value of GDP (NPV GDP) impact as the main macroeconomic indicator of AD disease burden. This accounts for the time value of money and so is the most relevant measure if the impacts are to be used for long-term investment planning.

The CGE model was calibrated using a 2011 Social Accounting Matrix (SAM) dataset for China which was extracted from the GTAP 9 database (GTAP, 2014). The static model was converted to a recursive-dynamic model by introducing factor updating equations, expanded to account for excess unskilled labor (until 2025) and fitted to a counterfactual growth path where growth rates decline linearly over time such that Chinese GDP per capita converges to predicted UK-levels in 2050, in accordance with the recent 2011–2014 decline in Chinese growth rates. The counterfactual solution for the model represents an annual series of business-as-usual snapshots of the Chinese economy for 2011–2050. AD burden scenarios were modelled as 'health shocks' to the economy (described below), i.e. they were removed from the counterfactual to result in an alternative set of snapshots, which was compared with the counterfactual to estimate the relative economic disease burden. More details on the CGE model and the SAM data set can be found in Appendix 2.

2.4. Modelling AD Economic Burden from AD Health Forecasts

In order to measure the macroeconomic burden of AD, it is important to accurately capture the main drivers. This analysis considered impacts on the labor force and public health system costs to be the main such drivers. Quantification of 'health shocks' were based on the AD model forecasts of prevalence and Disability-adjusted Life Years (DALYs) as measured by the sum of Years Lived with Disability (YLD) and Years of Life Lost (YLL) (see results below). The health forecasts were used to derive labor market and health budget shocks based on parameter values which are shown in Table 1. These parameter values highlight the focus of our model shocks on the loss of productive labor supply. Estimates suggest that 25.5% of informal caregivers lose time from work and that their work-time loss averages 0.246 work-years

Table 1
Parameter values for quantification of health-to-economy impacts.

	Disease Progression	
	Stage 1	Stage 2
1. Formal caregiving		
–work-time (work-years per AD patient-year)	0.125	0.185
2. Informal caregiving		
–Total time loss (years per AD patient-year)		
–Lower bound (PADL)	0.200	0.200
–Upper bound (PADL + IADL)	0.463	0.463
–Work-time loss (work-years per AD patient-year per caregiver)	0.246	0.246
–Informal caregivers with reduced work-time (%)	25.5%	25.5%
3. Non-care		
–Medical costs (US\$ per patient-year)	1,175	1,373
–Non-medical costs (US\$ per patient-year)	212	64

Source: own calculations based on published sources (Wang et al., 2008; Mould-Quevedo et al., 2013; Wimo et al., 2010). NB: PADL – personal activities of daily living; IADL – instrumental activities of daily living. Non-care medical costs consist of AD-related outpatient costs, inpatient costs, medication costs and physical therapy costs, non-care non-medical costs include transportation and special equipment. See appendices for additional information.

(Mould-Quevedo et al., 2013) implying, that the total informal work-time loss amounts to around 0.063 work-years per AD patient-year. Formal care requirements are estimated to be 0.125–0.185 work-years per AD patient-year in stages 1–2 based on cost estimates of formal caregiving (Wang et al., 2008).

In addition, Table 1 also presents upper and lower bounds on total informal time-loss per AD patient-year, allowing measurement of informal caregiver time loss at different intervals (see caregiver indicators in

Table 2). For more details on the quantification of ‘health shocks’, see Appendix 3.

3. Results

3.1. AD Health Burden

The future Chinese AD prevalence and health burden is illustrated in Fig. 1 for the period 2011–2050. Estimates of AD prevalence (Fig. 1a) increase rapidly from 5.9 million to 27.7 million with just over 55% of individuals in stage 1 in 2050. The 2013 prevalence estimate of 6.4 million is in broad agreement with the recently published 2013 overall dementia prevalence estimate of 10.5 million for East Asia (Prince et al., 2013).

The AD health burden, measured by DALYs (Fig. 1b), increases from 6.2 million to 22.4 million. The YLL share increases from 45% to 50% and the share of stage 2 YLDs declines from 30% to 25% over the 40 year period. Derived reductions in the effective labor force (Fig. 1c), which include direct health effects, and formal and informal caregiving, are estimated to grow from 0.37% of the Chinese workforce in 2011 to 1.16% in 2050. Non-care costs as a share of government budgets (Fig. 1d) decline over time due to conservative price-indexation of medical unit costs. These ‘health shocks’ were imposed on the macroeconomic model and results are presented in the next section.

3.2. AD Economic Burden

Table 2 presents the assessment of the AD economic burden, summarizing cumulative health and caregiver indicators, derived from the above AD health forecasts, and cumulative economic indicators in Net Present

Table 2
2011–2050 China AD disease burden (NPV; 8.0% p.a. discount rate).

Economic indicators		Cumulative NPV GDP (2011–2050; US\$ billion)	% of NPV GDP (2011–2050)	Share
	AD economic burden	7,962	1.25%	100.0%
	Decomposition 1			
	–Mortality	901	0.14%	11.3%
	–Stage 1	3,585	0.56%	45.0%
	–Stage 2	3,478	0.55%	43.7%
	Decomposition 2			
	Direct patient-specific labor force reduction			
	–Mortality	901	0.14%	11.3%
	–Morbidity	1,286	0.20%	16.2%
	Indirect caregiver labor force reduction			
	–Formal caregiving	1,924	0.30%	24.2%
	–Informal caregiving	798	0.13%	10.0%
	Other indirect costs			
	–Medical costs	2,731	0.43%	34.3%
	–Non-medical costs	319	0.05%	4.0%
Health indicators				
	AD prevalence	Cumulative case-years (2011–50; millions)	% of old-age population (age > 60)	
	Total prevalence	575	4.30%	
	–Stage 1	323	2.42%	56.1%
	–Stage 2	252	1.89%	43.9%
	AD health burden	Cumulative life-years (2011–50; millions)	% of old-age population (age > 60)	
	Total (= Δ DALY)	531	3.98%	
	– Δ YLL	244	1.82%	45.9%
	– Δ YLD	287	2.15%	54.1%
	Morbidity (= Δ YLD)			
	–Stage 1	132	0.99%	46.1%
	–Stage 2	155	1.16%	53.9%
Caregiver indicators				
	Informal caregiver time loss	Cumulative life-years (2011–50; millions)	% of cumulative life-years (all ages)	
	–PADL (lower bound)	57	0.11%	
	–PADL + IADL (upper bound)	133	0.24%	
	Caregiver work-time loss	Cumulative work-years (2011–50; millions)	% of cumulative work-years (all ages)	
	Total	63	0.22%	
	–Formal caregiving	45	0.16%	71.5%
	–Informal caregiving	18	0.06%	28.5%

Source: own simulations. NB: PADL – Personal Activities of Daily Living, IADL- Instrumental Activities of Daily Living.

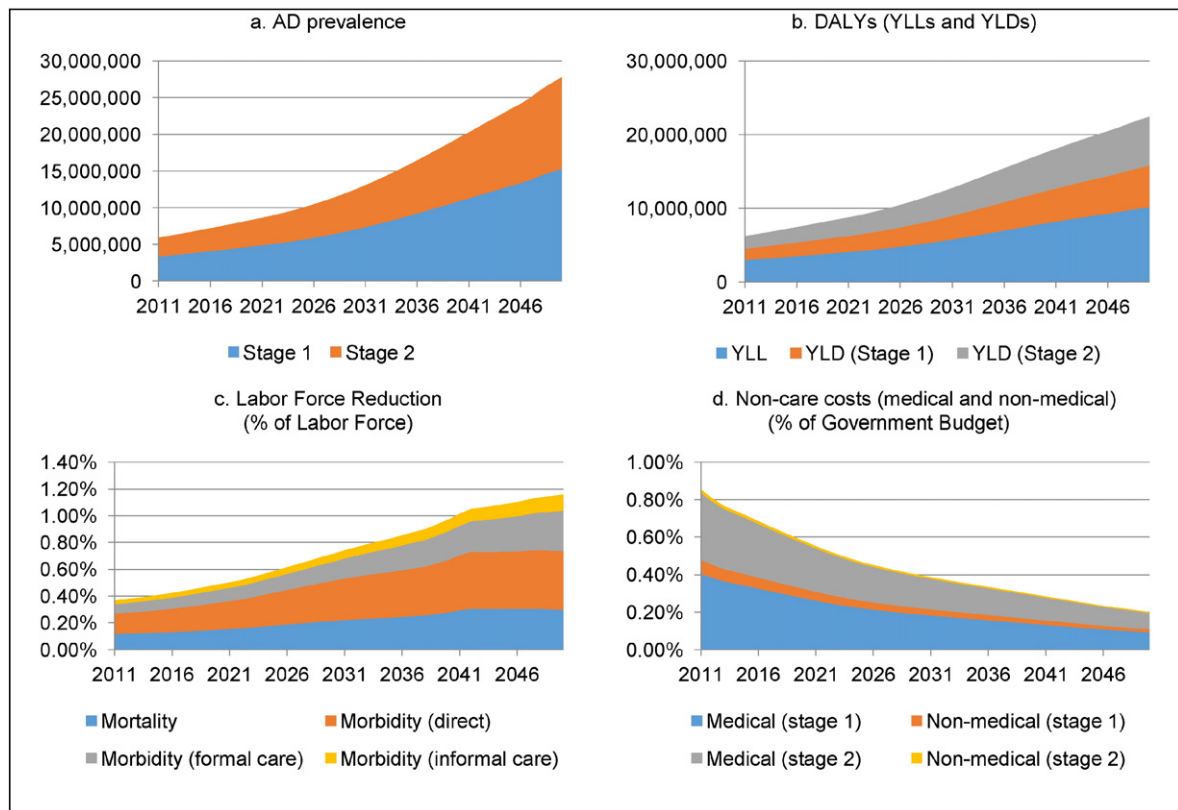


Fig. 1. Chinese AD disease-burden shocks.

Value (NPV) terms. At the extreme, the complete elimination of AD would increase the NPV of China's Gross Domestic Product (GDP) by US\$8.0 trillion between 2011 and 2050. Since previous valuations of the economic costs of AD use different methodologies and value the components of the economic disease burden differently, there are no directly comparable disease burden estimates. However, to set this figure in context, this cumulative 40 year impact is comparable to current estimates of China's GDP in 2012 (US\$8.1 trillion) and sufficient to fund one quarter of China's public health budget over the coming 40 years (currently 5.0–5.4% of GDP).

Decomposing the economic indicators in Table 2 illustrates the relative importance of the main drivers. Decomposition 1 indicates that morbidity effects (88.7%) exceed mortality effects (11.3%), while decomposition 2 indicates that morbidity impacts are primarily driven by medical costs (34.3%) and formal caregiving (24.2%). From a labor market perspective, the AD economic burden is driven relatively equally by three main categories of drivers, including direct patient-specific labor effects (28%), indirect caregiver labor effects (34%), and other indirect (medical) costs (38%). Labor market effects account for 62% of the overall economic burden. This illustrates the importance of accurate wage simulations for AD economic burden assessments.

The cumulative health indicators in Table 2 are consistent with the AD health burden results previously estimated and illustrate the large future AD burden for Chinese citizens. Over the coming 40 years 4.3% of the Chinese population aged over 60 are expected to develop AD, resulting in a 4.0% loss of DALYs attributable to AD. Labor effects from informal caregivers account for only 10% of the overall economic burden, but, with many more suffering the burden of care and distress, non-economic caregiver time loss among (older) caregivers is 3 to 7 fold (lower to upper bound) larger than the labor market time loss to the economy. Non-economic AD health burden indicators, including patient-specific functional loss and non-economic caregiver time loss, represent important complements to economic indicators from which decision makers can

assess human welfare implications of AD interventions and make investment decisions.

Accounting for population changes (Table 3) suggests that the economic disease burden amounts to US\$253 per capita per year. This suggests that the economic burden of AD will reduce the lifetime income of all members of the Chinese population, regardless of age, by nearly one percent, even after correcting for the time value of money. The NPV GDP impact per (living) patient case is estimated to be around US\$45,300.

The dynamic trajectory of the AD economic burden is presented in Fig. 2. For comparative and benchmark purposes, real GDP impacts (2011 US\$ prices) are presented in Fig. 2a–b, while NPV GDP impacts are presented in Fig. 2c–d. The economic burden, assessed by real GDP impact, grows exponentially from US\$15 billion (2011) to US\$1.07 trillion (2050). While methodologies differ, our 2050 macroeconomic simulation estimate is comparable in size to the COI-based 2050 prediction for the United States AD economic burden, of US\$1.10 trillion (2015-prices) (AA, 2015), indicating that China may converge with the US over the

Table 3

2011–2050 China AD economic burden per capita and per patient case-year (NPV; 8.0% p.a. discount rate).

	Avg. annual Δ NPV GDP per capita		Δ NPV GDP per patient case-year	
	US\$ (2011 NPV-values)	% of annual NPV GDP per capita	US\$ (2011 NPV-values)	% of total
Total	253.4	0.89%	45,328	
Decomposition 1				
–Mortality	–59.6	–0.21%	5,121	11.3%
–Stage 1	159.5	0.56%	20,416	45.0%
–Stage 2	154.7	0.55%	19,801	43.7%

Source: own simulations.

coming 40 years both in terms of economic (wage) conditions and AD health burdens.

The NPV GDP dynamic trajectories (Fig. 2c–d) of future AD economic burdens also grow exponentially. By 2050 the economic burden on the Chinese economy (US\$559 billion) will be more than 37 times that of 2011 (US\$15 billion). In addition, the decompositions of NPV GDP impacts illustrate the jump in economic disease burden in 2025 (when unskilled labor is no longer in excess supply), the equal long-term economic burden shares of stage 1 and 2 morbidity effects (decomposition 1), and also the increases in mortality share (from 1% in 2011 to 11% in 2050) and direct morbidity share (from 2% in 2011 to 16% in 2050), and the concomitant drop in medical burden share (from 63% in 2011 to 30% in 2050) (decomposition 2). The transition in burden shares reflects both the increasing importance of health and caregiving needs on the Chinese labor market and the declining medical expenses attributable to the conservative price-indexation of medical unit costs. If medical unit costs were to increase more rapidly over time, both the medical cost share and the overall economic disease burden, could increase considerably. Overall, the rapid and accelerating expansion of the AD economic burden reflects the importance of China's future demographic transition and development growth path over the coming 40 years. More detailed analysis of the dynamic effects is given in Appendix 4.

3.3. Sensitivity Analyses

Sensitivity analyses were performed on AD health model assumptions, formal and informal care ratios and macroeconomic model assumptions, and all assessments were made with reference to their cumulative NPV GDP impact. Variation in AD health model assumptions followed previous sensitivity analyses (Brookmeyer et al., 2007). Results were generally robust, but reduced AD incidence rates led to proportional NPV GDP burden reductions. Reductions in the ratio of formal to informal care (below current Shanghai levels) revealed that even extreme reductions

only reduce disease burdens by less than 5%. Results were also generally robust to variation in macroeconomic model assumptions, but reductions in upper working age (baseline: 79) reduced the NPV GDP burden by 10–24%, while reductions in the conservative discount rate (baseline: 8.0% p.a.) increased the NPV GDP burden by 31–129%. Our sensitivity analyses (relating to changes in stage transition, more rapid mortality following disease onset, and reduced incidence rates) suggest that beneficial changes in life-style related risk factors, similar to observed patterns in current European and US cohorts, could ease the disease burden towards the end of our time horizon, but any such changes are likely to have only small (proportional) impacts on economic outcomes, and prolonged continuation of current adverse Chinese trends could worsen economic outcomes. Details of the sensitivity analyses are presented in Appendix 5.

4. Discussion

The use of dual simulations in this study enables a comprehensive assessment of the twin AD health and macroeconomic disease burdens in China. The method combines health and macroeconomic modelling, and thereby allows for consistent assessment of the twin burdens, which are predicted to grow rapidly over the next 40 years. The models predict an oncoming AD epidemic in China where the health burden, measured by DALYs will more than quadruple over the coming 40 years, tripling the reductions in the effective labor supply attributable to AD-related health and care effects and imposing large losses on the macroeconomy. Despite conservative assumptions, including an 8% discount rate, the accelerating AD economic burden is predicted to equate to China's total GDP for 2012 (around US\$8.0 trillion). Over the next 40 years, the increasing generations of older Chinese citizens will impose an accelerating burden of AD care whilst increasing numbers of working-age AD cases draw an ever-growing number of individuals from their work, adding to the economic disease burden. As a result, the annual real GDP impact is also predicted to grow at an accelerating pace reaching US\$1.07 trillion in 2050 (2011-prices) and approaching

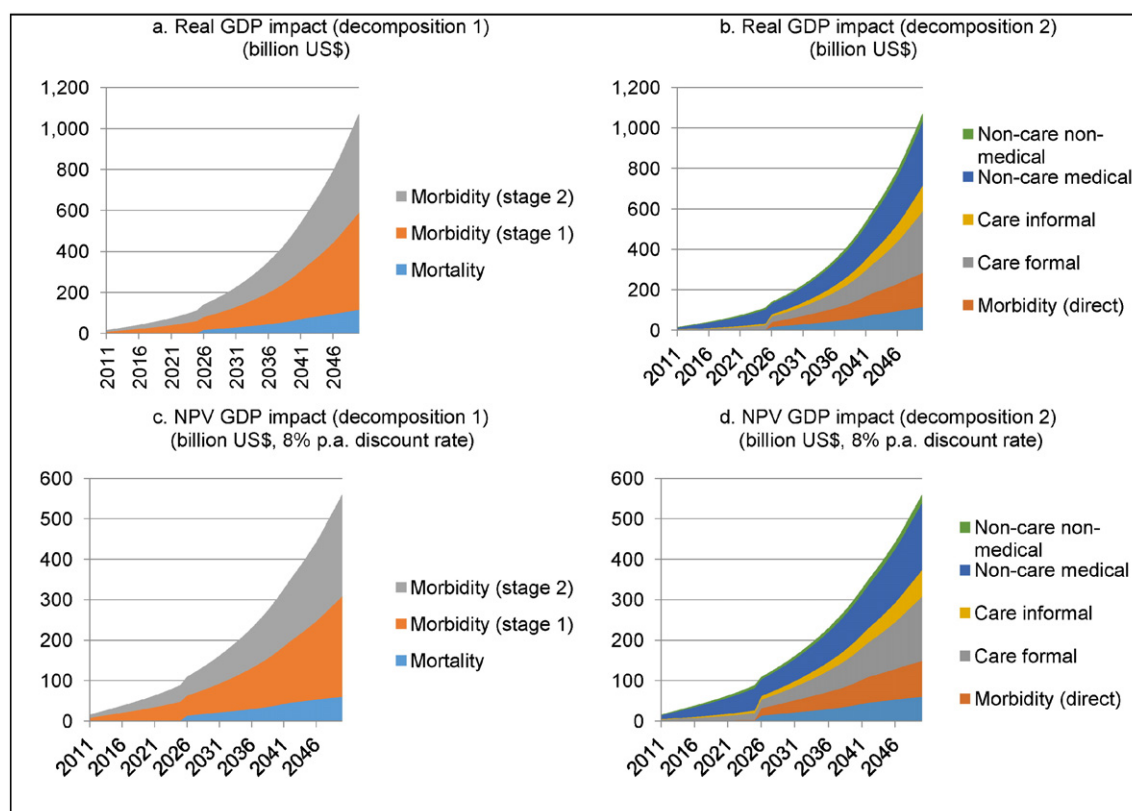


Fig. 2. Chinese AD disease-burden dynamic real and NPV GDP effects.

COI-based US predictions (2050: US\$1.10 trillion (2015–prices)) (AA, 2015).

Overall, the results suggest that the cumulative AD economic burden for China can be attributed equally to direct patient-specific labor effects, indirect caregiver labor effects, and indirect non-labor (medical) costs. Since 62% of the cumulative burden is attributable to direct and indirect losses of productive labor, which could be used for other purposes, estimates of the future economic impact of AD are critically dependent on accurate estimation of future wages. This result highlights the strength of the CGE approach. In contrast to existing COI-based studies, which use simple wage projections, CGE models capture dynamic wage and labor supply impacts and spillover effects across sectors. In this study, the macroeconomic CGE model determines wages from literature-based estimates of the future development growth path, the future labor market structure of China, and future AD health forecasts for China. This ensures a robust assessment of future Chinese wages and results in accurate estimates of labor supply impacts attributable to AD. In order to focus on monetary outcomes, our assessment of productive labor supply only monetizes informal caregiver time by employed caregivers, and thereby excludes valuation of non-productive leisure or household work time (which is more appropriately captured by non-economic caregiver indicators). In order to test the robustness of the results to variations in both macroeconomic and health assumptions, sensitivity analyses were carried out. The sensitivity analyses revealed that the economic disease burden is not very sensitive to the macroeconomic model assumptions about the future development path and future labor market structure. With the exception of halving incidence, which yielded a proportional 48.7% reduction in disease burden estimates, the results were also fairly insensitive to changes in disease model parameters.

The quantification of labor supply impacts in the macroeconomic CGE model is also distinct from the previous COI-based Shanghai-specific assessment which attributed 56% of costs per AD patient to informal caregiving (Wang et al., 2008). In contrast, since the approach employed in the CGE model only monetizes caregiving when it affects labor market participation, the CGE results suggest that just over 10% of the AD economic burden stems from labor lost due to informal caregiving. In order to not lose sight of the caregiver burden, the AD economic burden indicators were complemented with additional non-economic caregiver indicators on informal caregiver time use, and they show a 3–7 fold larger non-economic time burden on (older) caregivers compared to (working-age) labor-market time losses. While it is tempting to monetize unpaid caregiver time use to avoid complexity, it is critical to keep the economic and non-economic assessments separate, so policy makers can be fully informed about the multi-dimensionality of both monetary and other human welfare impacts.

Categorization of AD in the epidemiological simulations differs from some previous studies for China and the US (Wang et al., 2008; AA, 2015) which employed a three-state (mild, moderate, severe) categorization. The current two-state specification of AD (stage 1 and stage 2) encapsulates mild and moderate AD stages of previous studies as a single state (stage 1). In order to ensure conservative cost estimation, cost estimates from the literature for ‘mild’ AD were applied to stage 1 AD cases.

The holistic assessment of the health, caregiver, and macroeconomic burdens of AD in China should be of interest to both clinicians and policy makers, since it highlights both the increasing burden of AD to which health professionals and caregivers will be required to respond in the future, and the economic burden that could be avoided by successful policy-backed research and development of effective (medical and non-medical) interventions. Whilst the absence of similar macroeconomic analyses prevents like-for-like comparison with other disease burdens, the conservative approach employed, combined with the robustness of results under sensitivity analysis invites trust in the magnitude of the estimates presented. One question which has not been addressed in this study is the extent to which the effective treatment of co-morbid conditions will affect the burden of AD but this question

hinges upon the causal link between co-morbid conditions and AD which has still to be established (Poblador-Plou et al., 2014).

5. Conclusion

The combined health and macroeconomic assessment approach has important advantages over existing COI-based methods. Future AD health and economic burdens in China are significant, but the burden of AD impacts are clearly not limited to China, and further health and macroeconomic assessments of both AD disease burdens, and preventative and curative therapies, are required to shed further light on our results and to compare them with nations at other development levels, nations at other stages of demographic transition, and nations with other labor market structures. Research into combatting other chronic conditions should also be pursued and compared to AD assessments by using similar multi-dimensional health and macroeconomic methods. Nonetheless, the rapidly growing twin Chinese AD health and economic burdens suggest that investment in accelerated research programs for development of AD treatment and prevention interventions could bring large and accelerating commercial and society-wide human welfare gains over the medium to long term.

Funding and the Role of the Funder

This project was funded by an unrestricted grant from Janssen Research and Development, LLC. The sponsors of the study had no role in study design, economic data collection, data analysis or data interpretation. Simulations of AD disease scenarios were conducted by H.M. Arrighi, who is an employee of Janssen Research and Development LLC, using the published model and the parameters previously reported (Brookmeyer et al., 2007; Colantuoni et al., 2010; Stouthard et al., 1997). However, the analysis, views and opinions expressed in this paper are the authors' alone and do not necessarily represent the view of Janssen Research and Development, LLC. The corresponding author had final responsibility for the decision to submit for publication.

Acknowledgments

Authors' Contributions

MKB and HTJ led the conceptual development of the study, reviewed the literature, designed the macroeconomic modelling scenarios and selected the parameterization of the epidemiological scenarios. RDS provided advice and supervision throughout the project. HMA produced all AD simulations and provided advice on the epidemiological impacts. HTJ led with MKB in developing the CGE model and both HTJ and MKB performed the macroeconomic simulations and analyzed the results. MKB wrote the first draft of the paper, HTJ and RDS contributed to the intellectual guidance, analysis, and subsequent drafts of the report. All authors reviewed the report and provided further contributions and suggestions.

MKB and HTJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of interests

Dr. Keogh-Brown, Dr. Jensen and Dr. Smith report grants from Janssen Pharmaceutical Research and Development, LLC, during the conduct of the study; Dr. Arrighi reports other from Janssen Pharmaceutical Research & Development LLC, outside the submitted work.

Ethics Committee Approval

No ethical approval was required for this modelling study.

Appendix. Supplementary Data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ebiom.2015.12.019>.

References

- AA, 2015. Changing the Trajectory of Alzheimer's Disease: How a Treatment by 2025 Saves Lives and Dollars. Alzheimer's Association, Chicago.
- ADI, 2009. World Alzheimer Report 2009. Alzheimer's Disease International, London.
- ADI, 2014. World Alzheimer Report 2014. Alzheimer's Disease International, London.
- Banister, J., Hill, K.N., 2004. Mortality in China 1964–2000. *Popul. Stud.* 58 (1), 55–75.
- Brookmeyer, R., Gray, S., Kawas, C., 1998. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. *Am. J. Public Health* 88, 1337–1342.
- Brookmeyer, R., Johnson, E., Ziegler-Graham, K., Arrighi, H.M., 2007. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement.* 3, 186–191.
- Colantuoni, E., Surplus, G., Hackman, A., Arrighi, H.M., Brookmeyer, R., 2010. Web-based application to project the burden of Alzheimer's disease. *Alzheimers Dement.* 6, 425–428.
- Das, M., N'Diaye, P., 2013. Chronicle of a Decline Foretold: Has China Reached the Lewis Turning Point? IMF Working Paper WP/13/26 (January, <http://www.imf.org/external/pubs/ft/wp/2013/wp1326.pdf> (accessed June 24, 2015)).
- GTAP, 2014. 2011 China Social Accounting Matrix (Electronic Data). Global Trade Policy Analysis Project GTAP 9 database pre-release 2 (accessed 2 December 2014).
- Jensen, H.T., Keogh-Brown, M.R., Smith, R.D., et al., 2013. The importance of health co-benefits in macroeconomic assessments of UK Greenhouse Gas emission reduction strategies. *Clim. Chang.* 121, 223–237.
- Johnson, E., Brookmeyer, R., Ziegler-Graham, K., 2007. Modeling the effect of Alzheimer's disease on mortality. *Int. J. Biostat.* 3, 1–9.
- Langa, K.M., 2015. Is the risk of Alzheimer's disease and dementia declining? *Alzheimers Res. Ther.* 7, 34.
- Lock, K., Smith, R.D., Dangour, A.D., et al., 2010. Health, agricultural, and economic effects of adoption of healthy diet recommendations. *Lancet* 376, 1699–1709.
- Löfgren, H., Harris, R.L., Robinson, S., 2002. A Standard Computable General Equilibrium (CGE) Model in GAMS. International Food Policy Research Institute, Washington: DC.
- Matthews, F.E., Arthur, A., Barnes, L.E., Bond, J.J., et al., 2013. A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. *Lancet* 382, 1405–1412.
- Morris, J.C., 1993. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 43, 2412–2414 (2004).
- Mould-Quevedo, J.F., Tang, B., Harary, E., et al., 2013. The burden of caring for dementia patients: caregiver reports from a cross-sectional hospital-based study in China. *Expert Rev. Pharmacoecon. Outcomes Res.* 13, 663–673.
- Neumann, P.J., Araki, S., Arcelus, A., et al., 2001. Measuring Alzheimer's disease progression with transition probabilities: estimates from CERAD. *Neurology* 57, 957–964.
- Nussbaum, R.L., Ellis, C.E., 2003. Alzheimer's disease and Parkinson's disease. *N. Engl. J. Med.* 348, 1356–1364.
- Poblador-Plou, B., Calderón-Larrañaga, A., Marta-Moreno, et al., 2014. Comorbidity of dementia: a cross-sectional study of primary care older patients. *BMC Psychiatry* 14, 84.
- Prince, M.J., Acosta, D., Castro-Costa, E., Jackson, J., Shajii, K.S., 2009. Packages of care for dementia in low- and middle-income countries. *PLoS Med.* 6, e1000176.
- Prince, M., Guerchet, M., Prina, M., 2013. Policy Brief for Heads of Government: The Global Impact of Dementia 2013–2050. Alzheimer's Disease International, London.
- Qiu, C., von Strauss, E., Bäckman, L., et al., 2013. Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden. *Neurology* 80, 1888–1894 PubMed.
- Satizabal, C.L., Beiser, A., Chêne, G., et al., 2014. Temporal trends in dementia incidence in the Framingham study. *Alzheimers Dement.* 10. <http://dx.doi.org/10.1016/j.jalz.2014.04.4>.
- Smith, R.D., Keogh-Brown, M.R., Barnett, T., Tait, J., 2009. The economy-wide impact of pandemic influenza on the UK: a computable general equilibrium modelling experiment. *BMJ* 339, b4571.
- Sousa, R.M., Ferri, C.P., Acosta, D., et al., 2009. Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: a 10/66 Dementia Research Group population-based survey. *Lancet* 374, 1821–1830.
- Stern, Y., Tang, M., Albert, M.S., 1997. Predicting time to nursing home care and death in individuals with Alzheimer's disease. *JAMA* 277, 806–812.
- Stouthard, M.E.A., Essink-Bot, M.L., Bonsel, G.J., et al., 1997. Disability Weights for Diseases in the Netherlands. Department of Public Health, Erasmus University, Rotterdam.
- USCB, 2014. 2000–2050 China Population Projections (Electronic Data). US Census Bureau, Washington DC (accessed 11 August 2014).
- Wang, G., Cheng, Q., Zhang, S., et al., 2008. Economic impact of dementia in developing countries: an evaluation of Alzheimer-type dementia in Shanghai, China. *China J. Alzheimers Dis.* 15, 109–115.
- Wimo, A., Winblad, B., Grafstrom, M., 1999. The social consequences for families with Alzheimer's disease patients: potential impact of new drug treatment. *Int. J. Geriatr. Psychiatry* 14, 338–347.
- Wimo, A., Winblad, B., Jönsson, L., 2010. The worldwide societal costs of dementia: estimates for 2009. *Alzheimers Dement.* 6, 98–103.